IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PAR PHARMACEUTICAL, INC., PAR STERILE PRODUCTS, LLC, and ENDO PAR INNOVATION COMPANY, LLC,	)	
Plaintiffs,	)	C.A. No. 18-823-CFC-JLH
v.	)	
EAGLE PHARMACEUTICALS INC.,	)	
Defendant.	)	

PAR'S POST-TRIAL BRIEF REGARDING EAGLE'S INFRINGEMENT OF THE '209 AND '785 PATENTS

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INTRODUCTION

Two undisputed facts compel a finding of infringement in this case:

- First, Eagle's ANDA product has a drift problem: when stored in refrigerated conditions, its pH tends to rise. This is true even for batches made using Eagle's supposedly "optimized" manufacturing process.

- Second, per its release specification, Eagle seeks authority to release products into the marketplace with pH values up to 3.64, such that if those products drift upward just 0.01 pH unit—and the data shows they would drift far further—Eagle's products would rise into Par's claimed pH range.

These facts, taken together, mean that Eagle is seeking authority to sell products that would more likely than not infringe Par's patents. That is Hatch-Waxman Act infringement.

Eagle's arguments to escape infringement lack merit. Its principal contention is that changes to the manufacturing process guarantee that Eagle will not, in fact, release any products at the upper end of the release specification. That is legally irrelevant under controlling Federal Circuit precedent. The release specification is the gatekeeper for what Eagle will or will not be authorized to sell and thereby defines the scope of its authority under the ANDA.

But even if Eagle's "optimized" in-process specifications were relevant, they are inadequate to prevent release at the upper end of the pH range. Under Eagle's

"optimized" process, its ANDA products exhibit significant upward drift (as much as .07 pH units) between final in-process testing and release, which means that manufacturing at the upper end of the in-process specification of pH 3.54 will lead to release above 3.60, i.e., in the upper end of the release specification. With numerous batches showing upward drift following release of 0.04-0.06 pH units, drift into the infringing range is not only possible, but probable. Again, that is Hatch-Waxman infringement.

Eagle's reliance on its stability specification is equally unavailing. Periodic, post-sale testing of conformity to the stability specification will be conducted on an exceedingly small fraction of Eagle's commercial vials and would only detect infringement after-the-fact, contrary to the purpose of the Hatch-Waxman Act to prevent infringement before it occurs. Moreover, any approval by FDA of the stability specification would not reflect a determination as to the infringement issues presented here and would be made without the benefit of data demonstrating that Eagle's assurances to FDA that it has solved the drift problem are untrue.

Accordingly, Par is entitled to a judgment of infringement under § 271(e)(2), along with an order barring the FDA from approving Eagle's ANDA until after Par's patents expire. In the alternative, and at the very least, Par is entitled to a declaration under § 271(a) and (b) that products manufactured within the upper end of Eagle's release specification would infringe.

FACTUAL BACKGROUND

A. Eagle's ANDA Products Have A Drift Problem

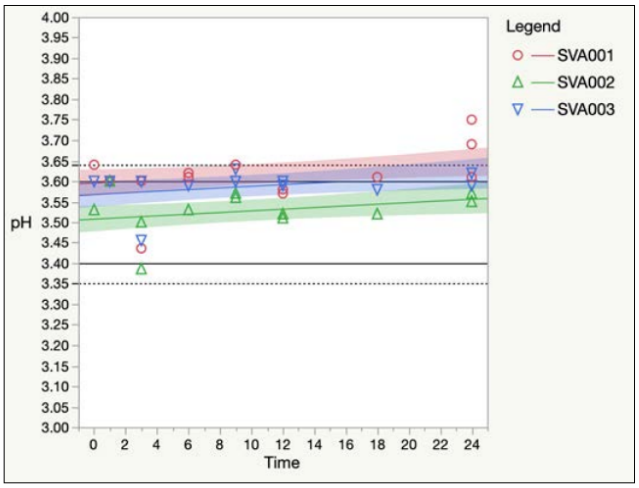
The evidence showed that Eagle's ANDA products had—***and still have***—a drift problem: the pH tends to rise over time when stored in refrigerated conditions.

That is why the first batch Eagle made (SVA001), which was manufactured at pH 3.64 on release, drifted into infringing territory. FOF55-57, 98.[1] That was Eagle's "Houston, we have a problem" moment.

Eagle investigated the cause, hoping to find a testing anomaly or operator error. Instead, multiple re-tests confirmed that the root cause was the product itself, such that manufacturing its product near the upper end of the ANDA's release specification would lead to infringement. FOF99-100; PTX-53, at AMRIVAS114548. Eagle prepared a statistical analysis and concluded that its registration batches exhibited a statistically significant upward drift in pH under refrigerated conditions, as shown in the following figure showing infringement (pH values $\geq$ 3.65) as early as 10 months into the products' shelf-life:

[1] Citations to "FOF__" refer to Par's accompanying Proposed Findings of Fact.

Figure 1: pH Results for the Registration Batches at 2-8°C for 24 Months



FOF101-103; PTX-1435, 9-10.

B. Eagle's "Optimized" Manufacturing Process Failed to Correct the Drift Problem

Faced with this drift problem, Eagle had two options to try to avoid infringement. It could either: (1) notify the FDA it was lowering the upper end of its release specification, formally binding itself to release at a lower pH; or (2) change its manufacturing process to eliminate the upward drift.

Eagle chose option (2). FOF105-106. It left its release pH specification unchanged but changed its in-process (post-filtration) pH specification to 3.42-3.54 and purportedly "optimized" its manufacturing process to better control pH. FOF72-79, 106. Eagle told the FDA that its in-process controls were "optimized to assure tighter control of pH is maintained during manufacturing," implying that it can never again release a batch with a pH at or near the upper end of its release specification. FOF106. Last month, Eagle reiterated that representation to FDA.

FOF105. Thus, Eagle has told—***and continues to tell***—FDA that it is able to "assure tighter control of pH" before releasing its products for commercial sale.

While Eagle is telling the FDA that it has solved the drift problem, the data adduced at trial tells another story. Eagle's products continue to exhibit upward drift and can drift into infringing territory, even when made using Eagle's "tightened"/"optimized" processes. FOF107-116. In particular:

- Data for the batches made according to Eagle's "optimized" process (SVA007-9, 11-14, 16-17) show a tendency for pH to rise between final in-process testing and release testing, by as much as 0.07 pH units, such that batches made at a pH within the latest in-process specification (up to 3.54) can rise to at least pH 3.61 by the time of release (FOF109-111);

  and

- Stability data for those "optimized" batches shows that pH continues to drift after release, by as much as 0.06 pH units, with significant drift occurring even within the first few weeks following release (FOF112-114);

  such that

- Products manufactured at or near the upper end of Eagle's in-process pH specification could be expected to drift into infringing territory during their shelf-life (FOF115-116).

Thus, Eagle's "optimized" process did not fix the drift problem and will not prevent Eagle from releasing products that fully meet its in-process testing and are still likely infringe Par's patents.

C. ANDA Specifications

The ANDA specification that determines the scope of products a generic can make and release for sale is the release specification. FOF80, 127. Prior to release, a generic may use in-process specifications that are intended to control the manufacturing process to "assure that the final product will meet its quality requirements"—*i.e.*, be manufactured to meet the release specifications. FOF75. The release specifications, in turn, are the tests and acceptance criteria that determine the suitability of a drug product at the time of its release for commercial sale. FOF80, 83, 127. Thus, the release specification is the gatekeeper for determining the scope of products Eagle can or cannot sell.

Stability specifications, by contrast, set forth criteria that drug products ***should meet*** throughout their shelf-life. FOF84. For FDA-approved products, conformity to stability specifications is assessed via periodic, post-sale testing conducted on a small fraction of products pulled from a subset of batches already released for sale. FOF85. Accordingly, stability specifications cannot prevent the sale of products that thereafter drift out-of-specification; they can only detect the existence of infringing products after-the-fact and only if the miniscule fraction of vials pulled for such testing includes products that have drifted into infringing territory. FOF127.

D. Eagle Will Be Authorized to Sell Infringing Products

No one disputed at trial that Eagle would be authorized to make and sell batches that pass both in-process and release testing.[2] The upper end of Eagle's release specification is pH 3.64, and numerous batches showed upward drift following release. FOF98-104, 112-116. Accordingly, the evidence was uncontested that release at the upper end of the pH range would result in drift into the infringing range. *Id*.

E. Eagle's Misplaced Reliance On In-Process Specifications

At trial, Eagle focused on its in-process specifications, arguing that because of its purported "optimization" of the manufacturing process, release at the upper end of the range could not happen. That is the wrong approach to Hatch Waxman infringement, which focuses on what Eagle would be authorized to sell. But even under Eagle's theory that these specifications matter, the available data shows that for products released at the upper end of the in-process specification, drift into the infringing range is not only possible, but likely.

[2] Eagle introduced deposition testimony from Ronald Aungst that AMRI would not release a batch that failed the in-process specifications but thereafter met release specifications. FOF83. Aungst's testimony was inconsistent on that point and is disputed by Par. FOF83. But, it is ultimately irrelevant, because Eagle indisputably would be authorized to sell batches that satisfy both in-process and release specifications, and products from such batches can be expected to infringe.

The evidence indisputably showed that products made within Eagle's in-process specification (up to pH 3.54) could be expected to drift into the upper end of its release pH specification (≥ pH 3.60). FOF107-111, 115. Accordingly, Eagle's "optimized" in-process specifications are no bar to release at a pH where the products would further drift into the infringing range during their shelf-life.

Moreover, Eagle's theory that a batch released within the in-process specifications could not infringe is not supported by actual stability data. ***None*** of the batches made using the supposedly "optimized" process were made at the upper end of Eagle's in-process pH specification—the highest value was pH 3.50, well below the upper limit of 3.54. FOF77-79, 122. Accordingly, Eagle has no stability data for a batch made via the "optimized" process at an in-process/post-filtration pH of 3.54, let alone data through the entire 24-month shelf-life. FOF122; *see* FOF61-69, 77-79. And the available data demonstrates that products made at that pH would be expected to drift upward, first into the upper end of Eagle's release specification, and then into infringing territory after release. FOF107-116.

Additionally, the data will not be vetted by the FDA. Eagle has only provided FDA with stability data for batches SVA001-009. FOF66, 69, 123. Thus, a significant portion of the data demonstrating that Eagle's supposedly "optimized" process failed to solve the drift problem and cannot be expected to

prevent Eagle's products from drifting into the infringing pH range during their shelf-life is not before the FDA and will play no role in its approval decision. *Id*.

F. Eagle's Inducement of Others' Infringement

At trial, Eagle did not dispute that Eagle's package insert would encourage and induce clinicians to use its ANDA products in accordance with the method of administration recited in the '209 patent claims. FOF132-133. Eagle will also induce infringement of the '785 patent by inducing clinicians to use its ANDA product at times when the product would be expected to have a pH between 3.7-3.9. FOF129-131.

ARGUMENT

I. GOVERNING LEGAL STANDARDS

Analyzing infringement involves two steps. *Markman v. Westview Instruments, Inc*., 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). The first is to construe disputed patent terms consistently with how they would be understood by POSAs. *Phillips v. AWH Corp*., 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). The second is to determine whether the accused product infringes the patent, by comparing it to the properly construed claims. *Markman*, 52 F.3d at 976. Infringement of a composition claim occurs when every claim element appears in the accused device. *Amgen Inc. v. F. Hoffman-La Roche Ltd*, 580 F.3d 1340, 1374 (Fed. Cir. 2009). For method claims, direct infringement occurs when all steps of the claimed method are performed by a single person.

Akamai Techs., Inc. v. Limelight Networks, Inc., 797 F.3d 1020, 1022 (Fed. Cir. 2015).

A. Hatch-Waxman Act Infringement

Under the Hatch-Waxman Act, it is an act of infringement to submit an ANDA seeking FDA-approval to make and sell a patented drug product. 35 U.S.C. § 271(e)(2); *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569-70 (Fed. Cir. 1997). "Although no traditional patent infringement has occurred until a patented product is made, used, or sold, under the Hatch–Waxman framework, the filing of an ANDA itself constitutes a technical infringement for jurisdictional purposes." *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1278 (Fed. Cir. 2013).

Once jurisdiction attaches, the "ultimate infringement question is determined by traditional patent law principles and, if a product that an ANDA applicant is asking the FDA to approve for sale falls within the scope of an issued patent, a judgment of infringement must necessarily ensue." *Id*. "What [the generic] has asked the FDA to approve as a regulatory matter is the subject matter that determines whether infringement will occur." *Id.* Thus, even if the generic "either tells the court that its manufacturing guidelines will keep it outside the scope of the claims or has even filed a declaration in the court stating that it will stay outside the scope of the claims," the generic is liable for infringement if "it has asked the

FDA to approve, and hopes to receive from the FDA, approval to market a product within the scope of the issued claims." *Id.* *See also Par Pharm., Inc. v. Hospira, Inc.*, 835 F. App'x 578, 586 (Fed. Cir. 2020) ("Even where internal documents suggest that a generic product will not meet a claim limitation in practice, representations about the ANDA's scope control the infringement analysis.").

Moreover, a patentee can succeed on a § 271(e)(2) claim by establishing that the approved ANDA products can be expected to infringe, even if strict conformity with the product specifications would indicate otherwise. *See, e.g.*, *Tyco Healthcare Grp. LP v. Mutual Pharm. Co., Inc.*, 762 F.3d 1338, 1344 (Fed. Cir. 2014) (the infringement inquiry "must be based on all of the relevant evidence *including* the ANDA" and the patentee may prove infringement if it "has evidence that the as-marketed commercial ANDA product will infringe"); *Bayer AG. v. Biovail Corp.*, 279 F.3d 1340, 1346-47 (Fed. Cir. 2002).

B. Induced Infringement

"[W]hoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). To prove inducement to infringe, the patentee must "establish[] that the defendant possessed specific intent to encourage another's infringement." *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006). Proof of intent can consist of evidence of active steps taken to encourage direct infringement, such as advertising an infringing use or instructing how to engage in

an infringing use. *Vanda Pharms. Inc. v. West-Ward-Pharms. Int'l Ltd.*, 887 F.3d 1117, 1129 (Fed. Cir. 2018); *Takeda Pharms. U.S.A. Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 630-631 (Fed. Cir. 2015). "[D]irect evidence is not required; rather, circumstantial evidence may suffice." *DSU*, 471 F.3d at 1306; *see also Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 644-645 (Fed. Cir. 2017).

C. Declaratory Relief Under § 271(a)

If the Court declines to issue a judgment under § 271(e)(4)(A) barring approval of Eagle's ANDA, Par would still be entitled to a declaration that the sale of products released at the upper end of the release specification (pH 3.60 or higher) would infringe. The Court has jurisdiction to grant relief under traditional patent law principles.

Courts may exercise jurisdiction over patent declaratory judgment actions when "the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118, 127 (2007) (quotation omitted). In *Lang v. Pacific Marine and Supply Co. Ltd.*, the Federal Circuit held that jurisdiction exists for claims of future infringement where the defendant has engaged in meaningful preparation to engage in allegedly infringing activity and is

on notice of the infringement accusations but has refused to change its course. 895 F.2d 761, 764 (Fed. Cir. 1990).

In ANDA cases, courts have exercised jurisdiction where, as here, the generic is systematically attempting to meet the applicable regulatory requirements and has expressed its intent to sell the accused product before patent expiration. *See, e.g., Glaxo*, 110 F.3d at 1571; *Bristol-Myers Squibb Co. v. Aurobindo Pharma U.S.A. Inc.*, 477 F.Supp.3d 306, 342 (D.Del. 2020) ("Under the circumstances present here—including the post-trial status of the case and the lack of any indication that Sigmapharm will delay its launch after FDA approval—the Court may properly exercise declaratory judgment jurisdiction.").

II. PAR IS ENTITLED TO A JUDGMENT OF INFRINGEMENT

Eagle stipulated that its ANDA product satisfies all limitations of the asserted claims, other than the pH limitations. As described above and in Par's Proposed Findings of Fact, the stability data and other evidence showed that if Eagle were to make batches within the upper end of its release pH specification, it is more likely than not that the pH of vials sold would drift into the infringing range during their shelf-life. In that event, Eagle would be both a direct infringer (via sale of infringing products) and an indirect infringer (via inducing use of infringing products by clinicians). Par is entitled to an order barring the FDA from

approving the Eagle ANDA and a declaration that sale of products manufactured at the upper end of the release specification would infringe.

A. Hatch-Waxman Act Infringement

1. Eagle Infringes under § 271(e)(2)

As summarized above, the Hatch-Waxman Act infringement inquiry assesses the scope of products the generic is seeking permission to sell and asks whether the manufacture and sale of those products would result in infringement. *Sunovion*, 731 F.3d at 1278 ("What [the generic manufacturer] has asked the FDA to approve as a regulatory matter is the subject matter that determines whether infringement will occur").[3]

Here, Eagle seeks permission to sell products made with a pH as high as 3.6 (including 3.64 rounded) at the time of release. FOF81. Indeed, Eagle's proposed package insert/label describes the product it intends to sell as having been "adjusted … to pH 3.4-3.6." FOF51, 119; PTX-1417 at EAGLEVAS0060906.[4]

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[3] At trial, there was extensive discussion about the identity of the RLD for Eagle's ANDA. While that issue is relevant to the FDA, whose approval decision will be based on considerations of safety and efficacy (including whether Eagle's product is "bioequivalent" to the RLD), the issues of patent infringement to be decided by the Court require a comparison of Eagle's ANDA product to Par's patent claims, rather than Par's commercial products. *See, e.g., Zenith Labs., Inc. v. Bristol-Myers Squibb Co.*, 19 F.3d 1418, 1423 (Fed. Cir. 1994).

[4] The "adjusted … to" language refers to adjustments made by the manufacturer during the manufacturing process, i.e., prior to its release for sale. FOF51.

Eagle does not dispute that its products show upward drift following release. Indeed, all but one of Eagle's "optimized" batches with available stability data showed upward drift following release. FOF112-114, 116; DTX-993.001. Three of the batches drifted 0.04 pH units within the first month after release. *Id.* (SVA007, 9, 13). Accordingly, it is beyond legitimate dispute that if Eagle is permitted to sell products with release values at the upper end of its range, infringing vials will be released into commerce. That is Hatch-Waxman Act infringement.

2. Eagle's "Optimization" Evidence Does Not Alter The Result

Eagle argues that notwithstanding the clear evidence of infringement, the Court should permit the FDA to approve the ANDA in light of changes Eagle has made to its in-process manufacturing protocol. Those arguments are legally irrelevant and factually unsupported.

First, Eagle asserts that its optimized process demonstrates that it has no intent to utilize the full scope of the release specification, but that line of argument is foreclosed by *Sunovion*. Even if Eagle "either tells the court that its manufacturing guidelines will keep it outside the scope of the claims or has even filed a declaration in the court stating that it will stay outside the scope of the claims," Eagle is liable for infringement if "it has asked the FDA to approve, and hopes to receive from the FDA, approval to market a product within the scope of

the issued claims." *Sunovion*, 731 F.3d at 1278. As in *Sunovion*, if Eagle has no intent to sell products within the upper end of its release specification, which would result in infringement, it "should not have requested, or should not accept, approval to market a product within the scope of the claim." *Id.* at 1279.

Par v. Hospira is also on point. Hospira argued that the ANDA infringement inquiry should focus on what it was likely, as a practical matter, to sell, rather than what its ANDA, if approved, would allow it to sell. 835 F. App'x. at 585. Relying on *Sunovion*, the Federal Circuit rejected that argument. *Id.* Thus, despite Hospira's insistence that the products it would actually make would not have the required amount of a "transition metal complexing agent," there was § 271(e)(2) infringement because the ANDA specified an upper limit for such an agent that would encompass the claimed range. *Id.* at 585-586.

The same is true here—Eagle's assertions that it will only make products in the middle of its pH specifications, and not utilize the full-breadth of its release pH specification, are legally irrelevant; it is what Eagle would be authorized to release for sale that matters.

Second, Eagle argues that as a factual matter, its "optimized" processes will prevent it from releasing at the upper end of the pH range. While *Sunovion* and *Par* teach that this is the wrong legal question, the evidence shows that Eagle's "optimizations" failed. In "optimized" batch SVA011, the final in-process reading

was pH 3.50, but prior to release, some of the vials increased to pH 3.57, an increase of 0.07. FOF107-111. In actual manufacturing, Eagle can use an in-process upper limit of pH 3.54, and adding 0.07 to that would put a commercial batch at pH 3.61, squarely within the upper range of the release specification. Eagle's factual claim that its new process makes it impossible to release in the upper end of the release specification is contradicted by the facts.

Third, Eagle clings to the paper release specification limit of pH 3.64, arguing that because that figure is outside the infringing range, evidence of real-world drift is irrelevant. The Federal Circuit has rejected that approach, recognizing that an ANDA product may start out within specification but later go out of specification, resulting in infringement.

Bayer AG. v. Biovail Corp., 279 F.3d 1340 (Fed. Cir. 2002), is on point. There, the ANDA specification required that the active ingredient have a "specific surface area" (SSA) above the claimed range. The Federal Circuit reversed summary judgment of non-infringement based on evidence that the active ingredient could meet the ANDA specification initially, but later fall within the claimed range once incorporated into finished products. This was despite a prior ruling in an earlier case involving a related ANDA to a product with a different dosage strength (30 mg), in which the Federal Circuit found non-infringement based on the ANDA specifications alone. In the later case, which involved a 60

mg product, the Federal Circuit held that "[e]ven assuming Elan strictly follows its 60 mg ANDA … in making a commercial tablet, Professor Antonietti's declaration raises a legitimate question as to whether Elan will likely make a 60 mg product that literally infringes Bayer's '466 patent upon approval of the ANDA." 279 F.3d at 1346-47. *See also Tyco*, 762 F.3d at 1344 ("it is not unreasonable for a patent owner to allege infringement under section 271(e)(2)(A) if the patent owner has evidence that the as-marketed commercial ANDA product will infringe, even though the hypothetical product specified in the ANDA could not infringe").

Here, the evidence shows that notwithstanding the fact that the pH of Eagle's products will be at or below 3.54 at the time of final in-process specifications (post-filtration) testing and below pH 3.65 at the time of release, the pH can and will drift upward over time. FOF109-116. As in *Biovail*, the fact that the product met specifications and would initially be non-infringing at the time it is released for sale is insufficient to avoid infringement if there is evidence—as there is here—that the product is likely to infringe at a later point in time.

3. The Root of the Problem is Eagle's Insistence on Maintaining a Release Specification Just Outside the Claimed Range

Throughout this litigation, Eagle has argued that SVA001 and any other evidence of infringement are outliers the Court should ignore. But the truth is that it is Eagle's insistence on maintaining a pH release limit that is just below the

infringing range that is the cause of the problem. Eagle has only itself to blame for its predicament.

Faced with the upward drift problem, Eagle has steadfastly refused to lower its release pH specification below 3.6 (3.64 rounded) as a way to create space between what it is seeking authority to sell and infringement of Par's patents. Eagle's refusal to do so speaks volumes about its true intent—it clearly wishes to reserve the right to sell products that, at the time of release, have a pH of 3.60 or higher, presumably because it knows that products made at the upper end of its in-process pH specification can drift into that range by the time of release testing. FOF81, 104-105, 109-111, 115. It is a fair inference from the evidence that Eagle wants the flexibility during full-scale manufacturing of hundreds of thousands of vials a year to be able to release such products for sale, even though they are likely to infringe Par's patents, rather than to have to throw out a batch following receipt of a release test outside the specification. *See* 21 C.F.R. § 211.165(f) (products that fail to meet the release specifications "shall be rejected").

Ferring B.V. v. Watson Labs., Inc.-Florida, 764 F.3d 1401 (Fed. Cir. 2014), a case on which Eagle relies heavily, is instructive on this point. There, the patent required a specified rate of dissolution of the active ingredient out of the tablet. *Id.* at 1403. Test data showed that finished, commercial tablets would only satisfy the dissolution limitation, and thereby infringe, if they had a "hardness of 17 kp or

greater." *Id.* at 1405. Accordingly, the district court "suggested at the close of trial that Watson could avoid infringement by submitting a 'change' of its ANDA to FDA," lowering the specification for hardness to something below 17 kp. *Id.* Watson took that suggestion and narrowed its hardness specification to a range of 13-16.5 kp (it originally was 13-20 kp), which the FDA thereafter approved. *Id.* at 1405-06. Based on the finding that tablets with a hardness below 17 kp would not infringe, and the fact that Watson's amended FDA-approved ANDA specification only allowed Watson to make and sell tablets with a hardness of 13-16.5 kp, the Federal Circuit reversed the district court's judgment of infringement.[5]

[5] The district court had found infringement based on two other pieces of evidence, which the Federal Circuit rejected: (1) evidence that experimental, uncoated core tablets tested during development of the product would satisfy the dissolution limitation, and (2) testing showing 4 tested samples met the limitation. *Id.* at 1405. As to the experimental, uncoated cores, the Federal Circuit held that the infringement inquiry focuses on the final, coated commercial tablets that Watson was approved to sell, so evidence about experimental, uncoated cores was irrelevant. *Id.* at 1409. As to the latter evidence, the testimony at trial was that the 4 samples with dissolution values within the claimed range were "atypical and aberrant" because "there was something incomplete about the coating" and the tablets "lacked coating integrity," as the coating "sort of came apart and opened up." *Id.* In other words, something anomalous happened during the manufacturing process that caused them to have a defective coating. The court held that the patentee could not rely on such manufacturing defects/anomalies to find infringement. *Id.* 1409-10. Here, by contrast, Eagle's own investigation of the out-of-specification result for SVA001 revealed that the upward drift into infringing territory was the result of the product itself (specifically, the pH value at the time of release), not any anomaly associated with particular vials. FOF98-103; Tr. 236:3-6.

When Eagle discovered the upward drift problem, it could have avoided infringement by lowering its release pH specification to a point at which the upward drift would no longer result in infringement, just as Watson lowered its hardness specification (after trial and at the court's suggestion). Eagle has refused to do so, however, and instead gambled that it could solve the problem with a supposedly "optimized" manufacturing process. That gamble failed—the data shows that even using the revised process, the upward drift problem still exists, and the pH of Eagle's products can ultimately still drift into infringing territory. Having gambled and lost, Eagle cannot complain about the result; Eagle's ANDA cannot be approved in its current form.[6]

4. Eagle's Stability Specification Will Not Prevent Infringement

Eagle argues that the Court cannot find infringement in view of its stability specification for pH of 3.4-3.6. That argument is flawed for numerous reasons.

[6] Eagle has previously cited *In re Brimonidine Patent Litigation*, 643 F.3d 1366 (Fed. Cir. 2011), but that case is inapposite. The generic's release pH specification was below the claimed range, and "[b]oth parties agree[d] that to the extent the pH of the formulation changes over time, it will fall, not rise." *Id.* at 1377. Thus, to the extent the pH drifted over time, it would drift further away from infringement, not into infringing territory. Here, the exact opposite is true. Thus, if anything, the case supports Par—if the specifications alone were dispositive, there would have been no need to look at the real-world pH evidence.

First, as Eagle confirmed, stability specifications set forth the criteria "that a drug product ***should meet*** throughout its shelf-life." D.I. 276 at 2 (emphasis added). The periodic, post-sale stability testing conducted on a small fraction of products pulled from a small subset of batches that have already been sold can only detect infringement after-the-fact, and only if the exceedingly small number of samples pulled for such testing includes products that have drifted into infringing territory. FOF85. That is inadequate to avoid a finding of infringement in the context of ANDA litigation, where the infringement inquiry is forward-looking and intended to resolve patent disputes while the ANDA is pending, before actual infringement occurs. *See, e.g., Vanda*, 887 F.3d at 1127; *Caraco Pharm. Labs., Ltd. v. Forest Labs., Inc.*, 527 F.3d 1278, 1283 (Fed. Circ. 2008).

In *Sunovion*, for example, the Federal Circuit found that "[t]he possibility that Sunovion could later test any of Reddy's commercially available generic eszopiclone products, when approved, and bring an infringement action under § 271(a), as Reddy argues, unnecessarily defers resolution of the infringement issue that the Hatch–Waxman framework was intended to address earlier, generally before ANDA approval." 731 F.3d at 1279. Moreover, as the Federal Circuit further pointed out, "it would be practically impossible for Sunovion, the FDA, or any court to monitor Reddy's compliance," so as to determine on an ongoing basis

whether Dr. Reddy's was complying with its internal manufacturing guidelines and pledge of non-infringement. *Id.*

Second, the issues before the FDA and this Court are different. Whether Eagle's product infringes Par's patents is not determined by the FDA; the FDA's concern is whether Eagle's product will be safe and effective. This Court is the tribunal that has the authority and responsibility to resolve Par's patent claims and protect Par from future infringement of its patents. There is no basis in the trial record or case law for this Court to defer judgment to the FDA on the issue of whether products manufactured by Eagle according to its "optimized" process can be expected to infringe at some point after they are released into the marketplace. Indeed, Eagle has submitted no data to FDA regarding any batch made at or near the upper end of its final in-process specification (pH 3.54) (FOF77-79, 122), and Eagle presented no expert or other evidence as to the extent to which FDA will evaluate the factual issues presented here in deciding whether to approve Eagle's ANDA. The issues of infringement presented here are for this Court to decide, not the FDA.

Third, this is particularly so because the evidence presented at trial is very different than the evidence Eagle has presented to the FDA. For example, the only stability data the FDA has regarding batches made with Eagle's "optimized" process is from batches SVA007-SVA009; FDA has ***no pH data*** for the later

batches Eagle also made using its "optimized" process. FOF63, 66, 69, 123. Thus, FDA does not have, for example, the evidence of significant pH variability among vials of Eagle's product at release (as shown by the inadvertent, duplicative release testing on SVA011), which demonstrates that Eagle's optimizations did not result in a more uniform and tightly controlled pH, as Eagle continues to represent is the case. FOF107-108. FDA also does not have significant portions of the data evidencing (a) the significant upward drift in pH between Eagle's final in-process and release testing and (b) the significant upward drift problem that Eagle's products continue to exhibit after release. FOF66, 69, 123. Moreover, FDA has not heard any of the expert evidence that this Court heard at trial, including the significant admissions by Dr. Park that these upward drifts are "representative of" the pH behavior for Eagle's future commercial batches. Tr. 461:8-12, 474:7-12.

Thus, while Eagle has told—***and continues to tell***—the FDA that it is now able to assure tight control of pH prior to release of its products for commercial sale, such that it will not release batches at or near the upper end of its release pH specification (like SVA001), the evidence presented at trial shows that Eagle's products still have a significant upward drift problem, and that Eagle's assurances to FDA are not true.

Fourth, the stability specification is not a legal bar to finding infringement. The Federal Circuit has recognized that tension between what is presented in an

ANDA submission and other, real-world evidence of the characteristics of the products to be sold upon approval can create disputed issues of fact that must be resolved by district courts.

In *Abbott Laboratories v. TorPharm, Inc.*, for instance, the Federal Circuit noted that "[i]t is also possible, at least in theory, that other evidence may directly contradict the clear representations of the ANDA and create a dispute of material fact regarding the identity of the compound that is likely to be sold following FDA approval." 300 F.3d 1367, 1373 (Fed. Cir. 2002). The Federal Circuit thereafter picked up on that in *Tyco*, holding that "it is not unreasonable for a patent owner to allege infringement under section 271(e)(2)(A) if the patent owner has evidence that the as-marketed commercial ANDA product will infringe, even though the hypothetical product specified in the ANDA could not infringe." *Tyco*, 762 F.3d at 1344.

Here, the evidence adduced at trial—including evidence not before the FDA—shows that (a) the pH of Eagle's product tends to drift upward when stored in refrigerated conditions (as is instructed on the label), and (b) the magnitude of the drift is sufficient to reach infringing territory from the upper end of Eagle's release specification. This is true notwithstanding the stability specification Eagle submitted with its ANDA, suggesting that the pH of its product "should" stay at

3.6 or below. Par is entitled to have this Court resolve its infringement claim based on the evidence presented to it.

In short, any approval of a stability specification for pH of 3.4-3.6 (which has not yet happened) would not prevent future infringement, would not reflect a determination as to the infringement issues presented here, and would be made without the benefit of much of the evidence presented at trial. Accordingly, that specification should not be treated as a barrier to a finding of infringement, and the Court should resolve the factual issues presented here, and adjudicate Par's patent claims based on the evidence presented at trial as to how Eagle's products, if sold, are likely to behave during their shelf-life.

B. Induced Infringement

In the Hatch-Waxman context, where the proposed label (a/k/a the package insert) instructs users to perform the patented method, the label may provide evidence of the ANDA applicant's affirmative intent to induce infringement. *Vanda*, 887 F.3d at 1129. In particular, the requisite intent to induce infringement can be inferred where following the instructions in the label would lead some users to practice the claimed method. *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010). That is exactly what we have here.

It is undisputed that if Eagle's ANDA products are used and administered as intended and instructed on the proposed package insert for the products, nurses and

medical professionals would perform the method of administration taught in Par's patents. FOF129. That can occur at any time during the products' shelf-life. FOF129. Clinicians do not test the pH of the products they administer, and do not know the pH of those products at the time of administration; they will simply administer the product at whatever pH the vial has at the time of administration. FOF130. And, if the product has a pH in the infringing range at the time of administration, the nurse will be a direct infringer. In that event, Eagle will have induced such direct infringement and be liable for induced infringement of the Asserted Claims (i.e., for having induced performance of the claimed method of the Asserted Claims of the '209 patent and use of the claimed formulations of the '785 patent). FOF129-136.

AstraZeneca is on point. The Federal Circuit affirmed a finding of specific intent to induce infringement based on the district court's findings that (1) "Apotex included instructions in its proposed label that that will cause at least some users to infringe the asserted method claims" and (2) "despite being aware of the infringement problem presented by the proposed label, Apotex nonetheless proceeded with its plans to distribute its generic drug product." 633 F.3d at 1060.[7]

[7] The issue was presented in the context of an appeal from entry of a preliminary injunction, and hence a finding that the patentee was likely to succeed on its induced infringement claim, rather than a final judgment as to inducement. *Id.* at

That is the exact situation we have here: (1) it was undisputed that Eagle's package insert/label instructs clinicians to administer Eagle's ANDA product in accordance with the claimed method of administration, and the label will therefore cause infringement any time that the vial provided to the clinician for administration to the patient has a pH within the claimed range; and (2) by virtue of this lawsuit and any finding of infringement entered by this Court, Eagle will be well aware of the infringement problem presented by the label.

As the Federal Circuit explained in *AstraZeneca*, "[t]he pertinent question is whether the proposed label instructs users to perform the patented method. If so, the proposed label may provide evidence of [the manufacturer's] affirmative intent to induce infringement." 633 F.3d at 1060. Although the product at issue in *AstraZeneca* could also be used in accordance with the label in non-infringing ways, Apotex would be liable for induced infringement because the instructions in the label would inevitably lead some users to practice the claimed method. So too here, although the administration of Eagle's products will not always infringe (i.e., when the vial is provided for administration with a pH outside of 3.7-3.9), given the products' upward drift problem, they will also inevitably be used at times when

1061. Nevertheless, *AstraZeneca* confirms that the evidence Par presented at trial is more than sufficient to prove Eagle's specific intent to induce infringement.

administration in accordance with the instructions on the label would infringe Par's patents.

In its Statement of Contested Issues of Law for the Final Pretrial Order, Eagle cited various cases for the proposition that mere knowledge of possible infringement by others is insufficient to demonstrate the specific intent necessary to support a claim for induced infringement. As the Court correctly noted during opening arguments, however, Hatch-Waxman Act cases present a different situation, because they involve an "artificial" act of infringement—the filing of the ANDA—and the focus of the case on future infringement in the event the FDA approves the sale of the proposed generic. *See* Trial Tr. at 100:20-103:23. Indeed, that is the very point the Federal Circuit made in *AstraZeneca*, where Apotex was found to have the requisite specific intent based on its decision to forge ahead and seek FDA approval to sell a product with a proposed label that instructed others to perform the claimed method, knowing that this would sometimes result in infringement.

The cases cited by Eagle in the context of ANDA cases are inapposite. The primary case on which Eagle relied is *Takeda Pharmaceuticals U.S.A., Inc. v. West-Ward Pharmaceutical Corp.*, 785 F.3d 625 (Fed. Cir. 2015). There, the alleged infringement was an "off-label" use of the product—i.e., the claim recited the use of colchicine to treat acute gout flares, but the use indicated on the label for the

accused product was for prophylactic treatment of gout. *Id.* at 629. Thus, the proposed label described non-patented uses of the accused product. *Id.* The Court noted that "mere knowledge of off-label infringing uses of [the accused product] would not establish inducement." *Id.* at 632.

Takeda is readily distinguishable, therefore, because here, the method of treatment recited in Par's patents (use of vasopressin to increase patients' blood pressure) is the very same treatment recited in Eagle's proposed label. Thus, whereas following the label at issue in *Takeda* would not result in performance of the claimed method, here it would. Indeed, *Takeda* expressly re-affirmed the holding in *AstraZeneca*, and distinguished it on the grounds that the alleged infringement required a use of the product outside of the method of treatment recited in the label.[8]

C. Section 271(a) and (b) Infringement

For similar reasons, Par is entitled to a declaration of infringement under § 271(a) and (b). Eagle has repeatedly told this Court that it expects to receive FDA-approval before year-end, and that a trial before then is necessary to avoid

[8] Eagle may point to the statement in the label describing the product as having been "adjusted … to" a pH of 3.4-.3.6 and argue that this means administering the product at a pH of 3.7 or higher is outside of the label. Not so. That language refers to pre-release pH adjustments made during the compounding process, and clinicians will administer them in accordance with the instructions on the label at whatever pH they happen to have at the time. FOF51.

emergency injunctive proceedings. May 26, 2021 Tr. at 17:5-21:13. Jurisdiction for such a declaratory judgment exists regardless whether Eagle's prediction of imminent FDA-approval proves to be true, as Eagle indisputably is continuing to take methodical and meaningful steps towards obtaining approval. *See Glaxo*, 110 F.3d at 1571. Indeed, Eagle has effectively conceded jurisdiction by asserting counterclaims alleging that the controversies regarding alleged infringement of the '209 and '785 patents are of "sufficient immediacy and reality" to warrant declaratory judgment. D.I. 136, ¶¶ 379, 404; *Ferring Pharms. Inc. v. Novel Labs., Inc.*, No. 17-894, 2018 WL 1583976, at *4 (D.Del. Apr. 2, 2018).

Accordingly, Par is entitled, at a minimum, to judgments declaring that Eagle's sale of products released with a pH at pH 3.60 or higher would result in direct infringement of the Asserted Claims, by Eagle itself (upon sale of the infringing products) or clinicians (upon use of the infringing products).

PAR'S REQUESTED RELIEF

Upon entry of findings of infringement as set forth above and in Par's Proposed Findings of Fact, submitted herewith, Par is entitled to an order, pursuant to 35 U.S.C. § 271(e)(4)(A), that the effective date of any approval of Eagle's ANDA shall not be earlier than the last expiration date of the Asserted Patents. Par is entitled to this order as a matter of right upon a finding of infringement under

§ 271(e)(2). *See* 35 U.S.C. § 271(e)(4)(A) ("the court ***shall*** order…") (emphasis added).[9]

In addition, and at the very least, Par is entitled to a declaration that Eagle's commercial manufacture and sale of products made with a pH upon release within the upper end of Eagle's proposed release pH specification (pH ≥ 3.60) would more likely than not result in infringement of the '209 and '785 patents, and that Eagle would be liable for such infringement, either directly (under § 271(a)) or indirectly (under § 271(b)).

Par is also entitled to recover its costs of suit. FED. R. CIV. P. 54(d).

CONCLUSION

The Court should enter judgment finding Eagle liable for infringing Par's patents and granting Par its requested relief.

[9] *In re Omeprazole*, 536 F.3d 1361, 1367-68 (Fed. Cir. 2008) (271(e)(4)(A) "provides an additional type of relief after a finding of infringement under section 271(e)(2) by ***requiring*** the district court to 'order the effective date of any approval of the drug…to be a date which is not earlier than the date of the expiration of the patent which has been infringed.'") (emphasis added).

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Respectfully submitted,

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CERTIFICATION OF COMPLIANCE

The foregoing document complies with the type-volume limitation of the Court's November 6, 2019 Standing Order. The text of this document was prepared in Times New Roman, 14 point. According to the word processing system used to prepare it, this document contains 7500 words, excluding letterhead, captions, and related non-substantive portions, compliant with the Court's limitations set forth at the close of trial. Trial Tr. 917:16-20.

/s/ Michael J. Farnan

Michael J. Farnan

Dated: July 19, 2021